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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|-------------------------------------|------------------|
| 10/601,692 | 06/24/2003 | Makiko Fliss | 001107.00357 | 7618 |
| 22907 7590 03/08/2007 BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051 | | | EXAMINER FREDMAN, JEFFREY NORMAN | |
| | | | ART UNIT | PAPER NUMBER |

1637

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|--|------------|---------------|
| 3 MONTHS | 03/08/2007 | PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| | | | |
|------------------------------|------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/601,692 | FLISS ET AL. | |
| | Examiner | Art Unit | |
| | Jeffrey Fredman | 1637 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 39,40 and 119-125 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 39,40 and 119-125 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some * c) ☐ None of:
 - 1. ☐ Certified copies of the priority documents have been received.
 - 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
 Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The objection to the disclosure is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112 – second paragraph

2. The rejection of claims 39, 40 and 118-126 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 39, 40 and 119-125 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As MPEP 2163.06 notes " If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

The amendment to claims 39 and 40 changing "302" to "303" represents new matter. There was no basis in the specification (which has been amended to be consistent with the new matter, but which had no previous basis for the new matter. Applicant argues that the change is based upon an "obvious error". Applicant attempts

to rely, in part, upon the attempt by the examiner to perform compact prosecution to support that the error is "obvious..

The legal standard for obvious errors, based on the MPEP 2163.07(II) and In re Oda is that "An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)." So two elements are necessary to correct the error, (1) the determination that the skilled practitioner would recognize the existence of error and (2) the determination that the skilled practitioner would recognize the appropriate correction. The cited case, In re Oda, states (see page 271, bottom of page to page 272) "Running through the foregoing discussion of the law is the clear and basic concept that the invention described in the original patent must not be changed. We note, first of all, that that is not a problem in this case. The invention before us, as defined in the claims, consists of three specific chemical compounds, there is no change proposed in the claims or in the description of the claimed compounds in the specification, there is no deviation whatever with respect to the invention."

From this discussion it is clear that when the invention (which is the claims) is at issue, it cannot be changed. In particular, the Oda court makes it clear that if the chemical compounds in the claims or specification were changed, this would be new matter. In Oda, the change was in how to make the chemical compounds and at page 272, it is clear that there were four independent bases to support an identification of the subject matter at issue.

The first part of the test is not met here because it was not clear that there was an error. This is evidenced by the 102(b) rejection over Genbank Accession No. V00662 which presumed that the base at position 302 represented a base that was already missing. This represented one reasonable interpretation of the claim. Consequently, there is no expectation that a skilled practitioner would have recognized the existence of an error. Second, the appropriate correction is even more speculative. It would only be by using information outside of the specification, information that is new matter, that one could determine that the sequence should have a deletion at position 303, and not represent an already deleted sequence, or a deletion at position 304, or a deletion at position 299, or a deletion at 311. For the second factor, even if the practitioner recognized that the sequence was flawed in some way, without exogenous information, the skilled practitioner would not be able to recognize the appropriate correction. Consequently, the error made in this application is not an obvious error, and the change which Applicant makes in the current claim set changes "the invention" in a way that the Court in In re Oda indicated would be new matter.

Specification

5. The amendment filed February 13, 2007 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The alterations which change the deletion from "302" to "303" represent new matter as discussed above.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Interpretation

6. Applicant argues that the term "oligonucleotide probe" must be limited to oligonucleotides in a range from 15 to 80 nucleotides based upon the citation of certain prior art references. This argument is easily rebutted by a review of patent applications which clearly use the term "oligonucleotide probe" to encompass sequences larger than the 715 nucleotides of Genbank Accession No. U 25391. For example, Lockhart et al (U.S. Patent 6,344,316) states "It is also recognized that the oligonucleotide probes can be relatively long, ranging in length up to about 1000 nucleotides (see column 20, lines 21-23)." Graham et al (U.S. Patent 6,379,943) notes "The detection oligonucleotide probes range in size between 10-1,000 bases (see column 13, lines 25-26)." In concord is Greenfield et al (U.S. Pub 2004/0023220) who notes "Generally, an oligonucleotide probe is less than about 1000 nucleotides in length (see paragraph 0060)." Yoshima (U.S. Patent 6,485,936) even discusses larger oligonucleotide probes, noting "The length of the oligonucleotide probe is usually 8 to 2000 bases (see column 8, lines 2-3)."

Therefore, a reasonable interpretation of the phrase "oligonucleotide probe" in light of the usage in patents and patent applications of the phrase would encompass the 715 nucleotide sequence of U25391 as an oligonucleotide probe.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. The rejection of claims 39, 40 and 118-126 under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. V00662 (1992) is withdrawn in view of the amendment.
9. The rejection of claims 39 and 40 under 35 U.S.C. 102(b) as being anticipated by Brennan et al (U.S. Patent 5,474,796) is withdrawn in view of the amendment.
10. Claims 39, 40 and 119-125 are rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession No. U25391 (1995).

This rejection relies upon the interpretation that SEQ ID NO: 1 lacks the deletion of the "C" base, and therefore only a run of 6 C bases is present. The run of 6 C bases is underlined. The query is Genbank Accession No. U25391 and the Sbjct is SEQ ID NO: 1.

Genbank Accession No U25391 teaches a sequence which has a deletion of a C relative to SEQ ID NO: 1 after position 302, and comprises 52 contiguous nucleotides identical to the delta 302 C deletion of SEQ ID NO: 1 as shown in the alignment below.

| | | |
|-------|-------------|--|
| Query | CTTTCCACACA | 599 |
| | | |
| Sbjct | CTTTCCACACA | 274 |
| Query | 600 | GACATCATAACAAAAAATTTCCACCAA <u>CCCCCT</u> CCCC |
| | | |
| Sbjct | 275 | GACATCATAACAAAAAATTTCCACCAAACCCCCCTCCCC |

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With regard to claims 29, 40 and 118-126, the sequence of Genbank Accession No. U25391 comprises more than 30 contiguous nucleotides of the mitochondrial genome identical to the delta 302 C deletion of SEQ ID NO: 1 as shown in the alignment above

11. Claims 39, 40 and 119-124 are rejected under 35 U.S.C. 102(b) as being anticipated by NEB catalog (1998/1999), pp. 121, 284.

The NEB catalog offered for sale a random primer mix of both 12 and 24 nucleotide primers. As the calculation below shows, about 3.2×10^8 molecules of every 12-mer and about 9 molecules of every single 24 mer are present in each tube of the 12 and 24 nucleotide mixtures, respectively.

a. Molecular weight of 12-mer:

$$12 \times 325 \text{ daltons/nucleotide} = 3,900 \text{ daltons} = 3,900 \text{ g/mol}$$

b. Total number of possible 12-mers:

$$4^{12} = 1.6 \times 10^7 \text{ molecules}$$

c. How many molecules of 12-mer in a vial sold by NEB:

$$1 \text{ A260 unit} = 33 \text{ mg} = 3.3 \times 10^{-5} \text{ g}$$

$$3.3 \times 10^{-5} \text{ g} \div 3,900 \text{ g/mol} = 8.4 \times 10^{-9} \text{ mol}$$

$$(8.4 \times 10^{-9} \text{ mol}) \times (6.02 \times 10^{23} \text{ molecules/mol}) = 5 \times 10^{15} \text{ molecules}$$

d. How many molecules of each 12-mer in a single vial:

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5×10^{15} molecules \div 1.6×10^7 molecules = 3.2×10^8 molecules of each 12-mer
per vial

e. Molecular weight of 24-mer:

24×325 daltons/nucleotide = 7,800 daltons = 7,800 g/mol

f. Total number of possible 24-mers:

$4^{24} = 2.8 \times 10^{14}$ molecules

g. How many molecules of 24-mer in a vial sold by NEB:

1 A260 unit = 33 mg = 3.3×10^{-5} g

3.3×10^{-5} g \div 7,800 g/mol = 4.2×10^{-9} mol

$(4.2 \times 10^{-9} \text{ mol}) \times (6.02 \times 10^{23} \text{ molecules/mol}) = 2.5 \times 10^{15}$ molecules

h. How many molecules of each 24-mer in a single vial:

2.5×10^{15} molecules \div 2.8×10^{14} molecules = 9 molecules/vial

With regard to claims 119-124, the NEB catalog vials will inherently and necessarily contain 24 nucleotide probes which comprise the claimed sequences. In the current situation, wherein the probe simply needs to overlap position 303, there are actually 47 different 24-mers which would overlap position 303, so there should be 47×9 or 423 24-mer molecules in the tubes sold by NEB in the 1998 catalog.

Response to Arguments

12. Applicant's arguments filed February 13, 2007 have been fully considered but they are not persuasive.

New Matter

Applicant first argues, preemptively, the new matter rejection. Applicant argues that the correction represents correction of an obvious error. As discussed in the rejection, the legal standard for obvious errors, based on the MPEP 2163.07(II) and In re Oda is that "An amendment to correct an obvious error does not constitute new matter where one skilled in the art would not only recognize the existence of error in the specification, but also the appropriate correction. In re Oda, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)." So two elements are necessary to correct the error, (1) the determination that the skilled practitioner would recognize the existence of error and (2) the determination that the skilled practitioner would recognize the appropriate correction. The cited case, In re Oda, states (see page 271, bottom of page to page 272) "Running through the foregoing discussion of the law is the clear and basic concept that the invention described in the original patent must not be changed. We note, first of all, that that is not a problem in this case. The invention before us, as defined in the claims, consists of three specific chemical compounds, there is no change proposed in the claims are in the description of the claimed compounds in the specification, there is no deviation whatever with respect to the invention."

From this discussion it is clear that when the invention (which is the claims) is at issue, it cannot be changed. In particular, the Oda court makes it clear that if the

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chemical compounds in the claims or specification were changed, this would be new matter. In *Oda*, the change was in how to make the chemical compounds and at page 272, it is clear that there were four independent bases to support an identification of the subject matter at issue.

The first part of the test is not met here because it was not clear that there was an error. This is evidenced by the 102(b) rejection over Genbank Accession No. V00662 which presumed that the base at position 302 represented a base that was already missing. This represented one reasonable interpretation of the claim. Consequently, there is no expectation that a skilled practitioner would have recognized the existence of an error. Second, the appropriate correction is even more speculative. It would only be by using information outside of the specification, information that is new matter, that one could determine that the sequence should have a deletion at position 303, and not represent an already deleted sequence, or a deletion at position 304, or a deletion at position 299, or a deletion at 311. For the second factor, even if the practitioner recognized that the sequence was flawed in some way, without exogenous information, the skilled practitioner would not be able to recognize the appropriate correction. Consequently, the error made in this application is not an obvious error, and the change which Applicant makes in the current claim set changes "the invention" in a way that the Court in *In re Oda* indicated would be new matter.

102(b) rejection over Genbank Accession No. U25391

Applicant argues that the probe size of U25391 is too large to be considered an oligonucleotide probe. This is an issue of claim interpretation. The Federal Circuit discussed claim interpretation by the PTO in In re Morris, where the Federal Circuit noted “[A]s an initial matter, the PTO applies to the verbiage of the proposed claims the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant’s specification.” In re Morris, 44 USPQ2d 1023, 1029 (Fed. Cir. 1997). In In re American Academy of Science Tech Center, 70 USPQ2d 1827, 1834 (Fed. Cir. 2004), the Federal Circuit noted “We have cautioned against reading limitations into a claim from the preferred embodiment described in the specification, even if it is the only embodiment described, absent clear disclaimer in the specification.”

Here, applicant cites to several works in the literature which discuss oligonucleotide probes in the range of 15 to 80 nucleotides. However, this evidence is directly rebutted in the claim interpretation section by four patents, which clearly indicate that the skilled practitioner recognizes that oligonucleotide probes can be as large as, at least, 2000 nucleotides.

Patents and applications, of skilled and inventive practitioners, routinely use the term “oligonucleotide probe” to encompass sequences larger than the 715 nucleotides of Genbank Accession No. U 25391. For example, Lockhart et al (U.S. Patent

6,344,316) states "It is also recognized that the oligonucleotide probes can be relatively long, ranging in length up to about 1000 nucleotides (see column 20, lines 21-23)." Graham et al (U.S. Patent 6,379,943) notes "The detection oligonucleotide probes range in size between 10-1,000 bases (see column 13, lines 25-26)." In concord is Greenfield et al (U.S. Pub 2004/0023220) who notes "Generally, an oligonucleotide probe is less than about 1000 nucleotides in length (see paragraph 0060)." Yoshima (U.S. Patent 6,485,936) even discusses larger oligonucleotide probes, noting "The length of the oligonucleotide probe is usually 8 to 2000 bases (see column 8, lines 2-3)."

Therefore, a reasonable interpretation of the phrase "oligonucleotide probe" in light of the usage in patents and patent applications of the phrase would encompass the 715 nucleotide sequence of U25391 as an oligonucleotide probe.

Conclusion

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any


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extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Jeffrey Fredman
Primary Examiner
Art Unit 1637

3/6/08